Sentara® Health Plans

SENTARA HEALTH PLANS CLINICAL PRACTICE GUIDELINE:

PERINATAL AND POSTPARTUM DEPRESSION

Guideline History

Date Approved	9/04
Date Revised	7/06, 3/08,1/10, 3/12, 3/14, 3/16, 3/18, 3/20, 3/22, 3/24
Date Reviewed	3/24
Next Review Date	3/26

Key Points

General:

✓ Discuss risks, benefits and alternatives. Document this discussion and the patient's consent to the treatment plan.

Depression:

- ✓ Depression is very common in women, especially in women of reproductive age. It is estimated that 14%-23% of pregnant women experience depression during pregnancy, and 5%-25% experiencedepression postpartum.
- ✓ Perinatal depression affects as many as one in seven women. The American College of Obstetricians and Gynecologists recommends all pregnant women be screened at least once during the perinatal period.
- ✓ SSRIs are allowed. to be continued. and./or initiated. during pregnancy.
- ✓ Significant risk factors for perinatal depression include personal or family history of depression; discontinuation of antidepressant prior to or during pregnancy; poor social support; marital or relationship problems; ambivalence about the pregnancy.
- ✓ The Edinburgh Postnatal Depression Scale (EPDS) has been 100% sensitive and 95.5% specific in detecting major postpartum depression at a threshold score higher than 13. Use of a formal screeningtool significantly increases the detection rate of antenatal depression. EPDS is being administered in the hospital, at the postpartum visits, and the pediatrician visits (well-baby visits).
- ✓ Risks of untreated depression during pregnancy may include lack of follow through with prenatal care, inadequate weight gain, preterm birth, and difficulty bonding with the unborn baby.
- ✓ For mild or moderate depression, psychotherapy alonemay be effective. In moderate to severe cases, treatment may include the use of antidepressant medications as well as counseling.
- ✓ Paroxetine use in pregnant women should be avoided, if possible. A fetal echocardiogram needs to be performed.
- ✓ Postpartum psychosis usually occurs within hours to days of delivery. Incidence is 1 in 1,known history 000 women overall, but 25-35% in women with a known history of bipolar disorder.
- ✓ Post-partum depression is a subset of major depressive disorder that meets the diagnostic criteria of major depressive disorder but occurs with onset during pregnancy or within 4 weeks of delivery. Suicide is the leading cause of death in the perinatal period (pregnancy and 1-year postpartum period) and accounts for about 20% of postpartum deaths.
- ✓ First-line treatment for mild-to-moderate postpartum depression is psychotherapy (cognitive or interpersonal therapy).
- ✓ The American College of Obstetricians and Gynecologist (ACOG), recommends SSRIs as first-line pharmacotherapy for women with moderate-to-severe postpartum depression.
- ✓ For women with no previous exposure to SSRIs or NRIs, sertraline and escitalopram are considered reasonable first-line agents. Highly protein-binding SSRIs such as sertraline may be used in women who are breastfeeding. SSRIs can take up to 12 weeks to provide relief. If there is any doubt about infant exposure TMS may be an alternative.

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Information for Providers on Antidepressants during Pregnancy and Breastfeeding – March 2023

This chart is produced by the University of Illinois at Chicago (UIC) by Illinois DocAssist as a summary of research on antidepressants in human pregnancy and breastfeeding

Antidepressants Risks in Pregnancy

Safety Data: No randomized control trials. Safety data derived largely from cohort studies, registry data, and prescription monitoring registries. Older studies suggested more adverse outcomes as they did not control for confounders such as presence and severity of maternal depression which is associated with adverse outcomes. Newer and better designed studies demonstrate less risks than previously believed.

Safety Ratings: Transition from Pregnancy Category (A, B, C, D, X) to PLLR (Pregnancy, Lactation, and Reproductive Labeling) as categories are confusing and did not accurately or consistently communicate differences in fetal risk. PLLR provides a risk summary based on available data in animal and human studies as well as clinical considerations for prescribers.

- **Obstetric Risks**
  - Both maternal depression and perinatal antidepressant use are associated with increased risk of Preterm Labor by 3 gestational days [1–3]
  - SSRI's are associated with increased risk of postpartum hemorrhage (reported incidence of postpartum hemorrhage ranges between 4-18% for SSRI exposure versus 3-11% for non-exposure in women with depression) [4]

- **Infant Risks**
  - **Congenital malformations** [1,5–7]
    - New and well-designed studies show no associated increased risk for congenital malformations (including cleft lip or cardiac defects)
  - **Persistent Pulmonary Hypertension of the Newborn**[8,9]
    - Slightly increased risk with late gestational antidepressant exposure however absolute risk is still very small
    - Magnitude of risk of PPHN is smaller than previously believed
    - No association between antidepressant exposure and severe PPHN (requiring respiratory intervention)
  - **Neonatal Adaptation** [10,11]
    - Risk of transient adaptation symptoms after delivery. Non-specific criteria so rates vary widely between studies
    - Symptoms if present are usually mild and include jitteriness, restlessness, irritability, increased muscle tone, sleep disturbance, feeding problems, and rapid breathing and spontaneously resolve
    - Discontinuing SSRIs shortly (2wks) before delivery does not appear to improve neonatal outcomes (Warburton et al 2010). Stopping Medication to decrease risks of adaptation syndrome is not recommended.
  - **Neurodevelopmental** [12–16]
    - New studies do not demonstrate an association between SSRI exposure and Autism Spectrum Disorder, Intellectual Disability or ADHD
    - Previous negative studies did not control for maternal/paternal depression which increases risk of ASD in offspring
    - Some studies suggested increased risk of motor delay in antidepressant exposed infants; however infants caught up before 24 months of age

March 23rd, 2023

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Antidepressant Risks in Breastfeeding [17–19]

Safety data: Includes limited studies examining relative infant dose, medication concentration in breastmilk, and infant plasma concentration as well as reports of adverse events

Safety rating:

- **Risks:** poor feeding, lethargy, irritability, not waking to feed, jitteriness, poor weight gain.
- Infants are exposed to much higher doses in-utero, therefore women should not be counseled to discontinue medications or not breastfeed due to low comparative exposure from breast milk; most SSRIs have undetectable serum concentrations in breastfeed infants
- Dr. Hale's Lactation Risk Categories L1-L5

  L1 SAFEST – Drug has been taken by many breastfeeding women without evidence of adverse effects in nursing infants OR controlled studies have failed to show evidence of risk.
  L2 SAFER – Drug has been studied in a limited number of breastfeeding women without evidence of adverse effects in nursing infants.
  L3 MODERATELY SAFE – Studies in breastfeeding have shown evidence for mild non-threatening adverse effects OR there are no studies in breastfeeding for a drug with possible adverse effects.
  L4 POSSIBLY HAZARDOUS – Studies have shown evidence for risk to a nursing infant, but in some circumstances the drug may be used during breastfeeding.
  L5 CONTRAINDICATED – Studies have shown significant risk to nursing infants. The drug should NOT be used during breastfeeding.

Clinical Considerations [3,20]

- No medication is risk free
- The risks of psychotropic use in pregnancy and lactation must be weighed with the risks of untreated or undertreated psychiatric illness to the mother and child
- In psychotropic naive women sertraline is the drug of choice in pregnancy and breastfeeding, followed by all other SSRIs other than paroxetine
- If a patient is pregnant and euthymic on a non-first line medication, the risk of changing medications (relapse of symptoms, multiple drug exposures in pregnancy) may outweigh the benefits for the mother-infant dyad.
- Untreated or undertreated depression is associated with preterm labor, preeclampsia, increased rates of substance use, suicide, impaired bonding and attachment with infant, postpartum depression, and risk of mental disorders in infant.
- Treatment target is remission of symptoms
- Drug metabolism in pregnancy may change due to alterations in enzymatic activity such as CYP 2D6 and 3A4 and increased creatinine clearance.[21,22] May consider supra-therapeutic doses in the context.

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SSRIs (Selective Serotonin Reuptake Inhibitors)[23]

- First line for perinatal and postpartum depression due to preferred safety data, tolerability, and efficacy
- SSRI's are amongst the most well studied medications in pregnancy
- Sertraline drug of choice in psychotropic naive women who are pregnant or breastfeeding
- Paroxetine 2nd line to other SSRI's given less favorable safety data and short half life

	Medication	Advantages	Disadvantages	Absolute Infant dose in breast milk (mg/d)	Lactation Rating *	Potential adverse effects of breastfeeding
SSRIs (Selective Serotonin Reuptake Inhibitors)	**Citalopram** (10-40mg) Increase in 10mg increments	• Few interactions with other medications		0.14	L2	
	Escitalopram (5-20 mg) Increase in 5-10 mg increments	• Few interactions with other medications • Less GI side effects than other SSRI's		0.04	L2	
	Fluoxetine (20-80 mg) Increase in 10-20mg increments	• First line for depressive symptoms in adolescents	• Higher incidence of neonatal adaptation syndrome than other SSRI's • Can be more activating than other SSRI's	0.14	L2	• Longer half-life less favorable than other SSRI's in breastfeeding
	Paroxetine (20-50mg) Increase by 10mg increments		• 2nd line to other SSRI's • Short half-life, increased risk of withdrawal with missed doses	0.03	L2	
	Sertraline (50-200 mg) Increase in 25-50 mg increments	• First choice for depression during pregnancy and breastfeeding in psychotropic naive women	• More GI side effects than other SSRI's	0.04	L2	

L1 SAFEST – Drug has been taken by many breastfeeding women without evidence of adverse effects in nursing infants OR controlled studies have failed to show evidence of risk. *
L2 SAFER – Drug has been studied in a limited number of breastfeeding women without evidence of adverse effects in nursing infants.
L3 MODERATELY SAFE – Studies in breastfeeding have shown evidence for mild non-threatening adverse effects OR there are no studies in breastfeeding for a drug with possible adverse effects.
L4 POSSIBLY HAZARDOUS – Studies have shown evidence for risk to a nursing infant, but in some circumstances the drug may be used during breastfeeding.
L5 CONTRAINDICATED – Studies have shown significant risk to nursing infants. The drug should NOT be used during breastfeeding

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SNRIs (Serotonin Norepinephrine Reuptake Inhibitors)[23,24]

- Second line to SSRI's in pregnancy and postpartum
- May be beneficial for patients with comorbid neuropathic pain
- Some studies show small increased risk of spontaneous abortion
- Rebound symptoms with missed doses
- Often require slow taper due to discontinuation symptoms (dizziness, nausea, headache, paresthesia, fatigue, vomiting, irritability, insomnia, diarrhea, anxiety, hyperhidrosis)

	Medication	Advantages	Disadvantages	Absolute Infant dose in breast milk (mg/d)	Lactation Rating*	Potential adverse effects of breastfeeding
SNRIs (Serotonin Norepinephrine Reuptake Inhibitors)	**Desvenlefaxine**[27] (50mg)	• Also treats neuropathic pain • Absolute infant dose in breastfeeding half that of venlafaxine	• Least studied of the SNRI's	.016	L3	
	Duloxetine (60mg-120mg) Start 40mg, increase 20-30mg/day increments per week	• Also treats neuropathic pain and fibromyalgia • Can be given in two divided doses to aid tolerability	• Less studied than Venlafaxine in pregnancy • Small increased risk of miscarriage	<0.03	L3	
	Venlefaxine XL (37.5- 225 mg) increase in 37.5mg increments	• Also treats neuropathic pain at higher doses • More studied than other SNRI's in pregnancy	• Small increased risk of miscarriage • Higher rates of discontinuation symptoms than duloxetine	0.5	L2	

L1 SAFEST – Drug has been taken by many breastfeeding women without evidence of adverse effects in nursing infants OR controlled studies have failed to show evidence of risk. *
L2 SAFER – Drug has been studied in a limited number of breastfeeding women without evidence of adverse effects in nursing infants.
L3 MODERATELY SAFE – Studies in breastfeeding have shown evidence for mild non-threatening adverse effects OR there are no studies in breastfeeding for a drug with possible adverse effects.
L4 POSSIBLY HAZARDOUS – Studies have shown evidence for risk to a nursing infant, but in some circumstances the drug may be used during breastfeeding.
L5 CONTRAINDICATED – Studies have shown significant risk to nursing infants. The drug should NOT be used during breastfeeding.

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Non-SSRIs (Selective Serotonin Reuptake Inhibitors)/SNRIs (Serotonin Norepinephrine Reuptake Inhibitors)

	Medication	Advantages	Disadvantages	Absolute infant dose in breast milk (mg/d)	Lactation Rating*	Potential adverse effects of breastfeeding
Non-SSRIs/SNRIs	**Buproprion[25] Buproprion Registry XL** (150-450 mg) Increase in 150mg increments	• Fewer sexual side effects than SSRI's or SNRI's • Less risk of weight gain • Aids smoking cessation • Does not appear to be associated with increased risk of congenital malformations in limited studies	• Not recommended in those with eating disorders or seizure disorders • Decreases seizure threshold • May sometimes worsen anxiety	0.20	L3	• Sleep disturbance of infants reported • Isolated case reports of infant seizure
	Mirtazapine[26] (15-45mg) Increase in 15 mg increments	• Aids with sleep and promotes appetite	• Sedating • Less studied than SSRIs	0.04	L3	
	Nortriptyline (100-150 mg daily) Start 25mg daily increase in 25mg increments	• Can also be used for migraine prophylaxis	• Maternal side effects additive to pregnancy effects (sedation, constipation, tachycardia) • Orthostatic hypotension, risking decreased placental perfusion • Fetal and neonatal side effects: tachycardia, urinary retention	0.07	L2	• Dry mouth, constipation, urinary retention

L1 SAFEST – Drug has been taken by many breastfeeding women without evidence of adverse effects in nursing infants OR controlled studies have failed to show evidence of risk. *
L2 SAFER – Drug has been studied in a limited number of breastfeeding women without evidence of adverse effects in nursing infants.
L3 MODERATELY SAFE – Studies in breastfeeding have shown evidence for mild non-threatening adverse effects OR there are no studies in breastfeeding for a drug with possible adverse effects.
L4 POSSIBLY HAZARDOUS – Studies have shown evidence for risk to a nursing infant, but in some circumstances the drug may be used during breastfeeding.
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Two new treatment options:

1. In 2019 the FDA approved brexanolone (Zurlesso), an intravenous injection, the first treatment specifically for postpartum depression. Brexanolone is fast acting (improvement in 2.5 days) but requires patients to be hospitalized for a 60 hour - long infusion, during which they must be monitored for excessive sedation and loss of consciousness. Additionally, its cost before discounts and insurance is $ 34,000 per treatment.

2. 2. In August 2023, the FDA approve zuranolone (Zurzuvae), an oral pill formulation that is far more convenient to take. Zuranolone is a neuroactive steroid that is a positive modulator of the GABAa receptor. However, it will carry a boxed warning not to drive a motor vehicle or engage in potentially hazardous behavior. Costs before discounts and insurance are $ 15,900 for two weeks of treatment or $1,135 per pill. There are symptoms of withdrawal after stopping the drug, that include insomnia, palpitations, decreased appetite, hyperhidrosis, and paranoia.

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Edinburgh Postnatal Depression Scale[1] (EPDS)

Name: _____ Address: _____

Your Date of Birth: _____ _____

Baby's Date of Birth: _____ Phone: _____

As you are pregnant or have recently had a baby, we would like to know how you are feeling. Please check the answer that comes closest to how you have felt **IN THE PAST 7 DAYS**, not just how you feel today.

Here is an example, already completed.

I have felt happy:
- ☐ Yes, all the time
- ☒ Yes, most of the time
- ☐ No, not very often
- ☐ No, not at all

this would mean: "I have felt happy most of the time" during the past week. Please complete the other questions in the same way.

In the past 7 days:

1. I have been able to laugh and see the funny side of things
   - ☐ As much as I always could
   - ☐ Not quite so much now
   - ☐ Definitely not so much now
   - ☐ Not at all

2. I have looked forward with enjoyment to things
   - ☐ As much as I ever did
   - ☐ Rather less than I used to
   - ☐ Definitely less than I used to
   - ☐ Hardly at all

*3. I have blamed myself unnecessarily when things went wrong
   - ☐ Yes, most of the time
   - ☐ Yes, some of the time
   - ☐ Not very often
   - ☐ No, never

4. I have been anxious or worried for no good reason
   - ☐ No, not at all
   - ☐ Hardly ever
   - ☐ Yes, sometimes
   - ☐ Yes, very often

5. I have felt scared or panicky for no very good reason
   - ☐ Yes, quite a lot
   - ☐ Yes, sometimes
   - ☐ No, not much
   - ☐ No, not at all

*6. Things have been getting on top of me
   - ☐ Yes, most of the time I haven't been able to cope at all
   - ☐ Yes, sometimes I haven't been coping as well as usual
   - ☐ No, most of the time I have coped quite well
   - ☐ No, I have been coping as well as ever

*7. I have been so unhappy that I have had difficulty sleeping
   - ☐ Yes, most of the time
   - ☐ Yes, sometimes
   - ☐ Not very often
   - ☐ No, not at all

*8. I have felt sad or miserable
   - ☐ Yes, most of the time
   - ☐ Yes, quite often
   - ☐ Not very often
   - ☐ No, not at all

*9. I have been so unhappy that I have been crying
   - ☐ Yes, most of the time
   - ☐ Yes, quite often
   - ☐ Only occasionally
   - ☐ No, never

*10. The thought of harming myself has occurred to me
   - ☐ Yes, quite often
   - ☐ Sometimes
   - ☐ Hardly ever
   - ☐ Never

Administered/Reviewed by _____ Date _____

[1]Source: Cox, J.L., Holden, J.M., and Sagovsky, R. 1987. Detection of postnatal depression: Development of the 10-item Edinburgh Postnatal Depression Scale. *British Journal of Psychiatry* 150:782-786.

[2]Source: K. L. Wisner, B. L. Parry, C. M. Piontek, Postpartum Depression N Engl J Med vol. 347, No 3, July 18, 2002, 194-199.

Instructions for Using the Edinburgh Postnatal Depression Scale[1] (EPDS)

The 10-question Edinburgh Postnatal Depression Scale (EPDS) is a valuable and efficient way of identifying patients at risk for perinatal depression.

It is a proven screening tool.

It is easy to administer.

It can be completed at home and brought to a physician's office (OB, Pediatric, Family Practice) or the office of a mental health practitioner.

It can also be downloaded in the medical setting.

The scale indicates how the woman has felt ***during the previous week***.

It may be useful to repeat the screen in 2 weeks in questionable cases.

The EPDS score should inform but not override clinical judgment as a complete and thoughtful clinical assessment should be carried out to confirm the diagnosis.

Instructions for using the Edinburgh Postnatal Depression Scale:

1. Ask the woman to check the response that comes closest to how she has been feeling in the previous 7 days.
2. All items must be completed.
3. The mother should complete the scale herself, unless she has limited English or has difficulty with reading. She should not discuss her answers with others.

SCORING

A score of greaterthan 13 as a threshold value is:

100% sensitive, 95.5% specific for PPD[2]

Possible Depression: 10 or greater

Always look at item #10 for suicidal thoughts.

Responses are scored 0, 1, 2, or 3 according to increased severity of symptom. Items marked with an asterisk (*) are reverse scored (i.e., 3, 2, 1, and 0). The total score is determined by adding together the scores for each of the 10 items.

Good clinical care also involves asking if the mother has fears about hurting the baby or fears of the baby coming to harm.

[1]Cox, J.L., Holden, J.M., and Sagovsky, R. 1987. Detection of postnatal depression: Development of the 10-item Edinburgh Postnatal Depression Scale. *British Journal of Psychiatry* 150:782-786.

[2]Boyce, P. Stubbs, J., and Todd, A. 1987. The EPDS: validation for an Australian sample. Aust N Z J Psychiatry 27:472-6.

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Concerns That May Limit the Use of Zuranolone. Prasad V, Allely D JAMA Vol 331,No 2 January 9, 2024

A Fast-Acting Pill received Approval for Postpartum Depression-Is It a Game Changer? Rubin R JAMA Network August 23, 2023

Resources

American Psychological Association. Brochure: *Postpartum Depression* May be downloaded from https://www.apa.org/pVwomen/resources/reports/postpartum-depression-brochure-2007.pdf

The American College of Obstetricians and Gynecologists http://www.acog.org

The American College of Obstetricians and Gynecologists. *Postpartum Depression.* Patient educational Pamphlet AP0 91. Washington, DC:American College of Obstetricians and Gynecologists; 2013.
Print copies can be ordered online at http://sales.acog.org or by calling 1-800-762-2264.

Massachusetts General Hospital Center for Women's Health: Reproductive Psychiatry Resource and Information Center. Psychiatric Disorders During Pregnancy
http://www.womensmentalhealth.org/specialty-clinics/psychiatric-disorders-during-pregnancy

Massachusetts Child Psychiatry Access Project (MCPAP) for Moms Toolkit available at https://www.mcpapformoms.org/Toolkits/Toolkit.aspx

Postpartum Support International. 6706 SW 54th Avenue, Portland, OR 97219. (503) 894-9453. Available at http://www.postpartum.net Support Helpline: 1-800-9444PPD (4773)

The 2020 Mom Project website: http://www.2020mom.org/

US Department of Health and Human Services; Health Resources & Services Administration, 2010. *Depression during and After Pregnoncy: A Resource for Women, Their Famiies, and Friends.* Patient educational brochure.
Available online at www.mchb.hrsa.gov/pregnancyandbewnd/depression
Print copies can be obtained from the HRSA Information Center 1-888-Ask-HRSA.

Postpartum Support International (PSI) website: https://www.postpartum.net/professionals/screening/